

The human family tree and the Neandertal branch

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Abstract

We consider a large population of asexually reproducing individuals in absence of selective pressure. The population size is maintained constant by the environment. We find out that distances between individuals (time from the last common ancestor) exhibit highly non trivial properties. In particular their distribution in a single population is random even in the thermodynamical limit. As a result, not only distances are different for different pairs of individuals but also the mean distance of the individuals of a given population is different at different times. All computed quantities are parameters free and only scale linearly with the population size. Results in this paper may have some relevance in the 'Out of Africa/ Multi-regional' debate about the origin of modern man. In fact, the recovery of mitochondrial DNA (mtDNA) from Neandertal fossils in three different loci: Feldhofer (Germany), Mezmaiskaya (Northern Caucaso), Vinjia (Croatia), permitted to compare Neandertal/Neandertal distances with Neandertal/modern and modern/modern ones.

In 1997 a team of researchers [1, 2] announced that mtDNA was extracted from the humerus of the first recognized Neandertal fossil, the individual found at the Feldhofer cave in the Neander Valley in Germany in 1856. In 1999 and 2000 mtDNA had been extracted from a second Neandertal, a 29,000 year-old fossil of a baby recently discovered in Mezmaiskaya cave in south-western Russia and from a third Neandertal specimen from a cave at Vindija, Croatia [2].

More recently, another team [3] extracted mtDNA from a 60,000 year-old fossil of an anatomically modern human discovered in the dry bed of Lake Mungo in New South Wales, Australia.

What makes mtDNA interestingly different from nuclear DNA is that it is inherited only from the mother. In principle, every lineage can be followed until the woman whose mtDNA is the common ancestor of the mtDNA of all living humans. This hypothetical woman is known as mitochondrial Eve.

More sketchy, we can say that mtDNA reproduces asexually since there is not recombination as for nuclear DNA. Therefore, assuming that the mtDNA mutates at a constant rate, the number of differences in mtDNA between two individuals is a measure of their distance, i.e. the number of generations from the common ancestor. This is particularly true for the previously mentioned studies, since the part of mtDNA concerned is the hypervariable region which seems to mutate in absence of selective pressure.

On the basis of the comparison with the mtDNA of living humans, it was argued that both Neandertals and Mungo man, should be eliminated from our ancestry. In fact, the distance of Neandertal from living humans was estimated to be more than three times the average difference between living Sapiens or between the three Neandertals. Moreover, Mungo man seems to carry a mtDNA which disappeared from modern humanity.

In order to decide if these conclusions are correct we have to understand if these differences have statistical relevance. We address here to this problem by means of a very general model without need to specify the details of the dynamics.

We assume that the population size is constantly of N individuals due to ecological or environmental factors. At any generation we have N new individuals which replace the N individuals of previous generation. Since we deal with mtDNA, the reproduction is asexual and any individual of the new generation has a single parent in the previous one. Obviously, the average number of offsprings of an individual in the old generation is one, nevertheless,

some of them will not have any offspring and others will have more than one.

We do not fix here the stochastic rule assigning the number of offsprings to any individual since results do not depend on the dynamics details. The only requirement is that the probability that two individuals in the new generation have the same parent is of the order of $1/N$ for large N . This is a very weak and reasonable assumption: just think at our life experience. To be more clear, we make two examples of stochastic rules which satisfy this requirement. The first rule is that at any generation one half of the individuals (chosen at random) has no offsprings and the remaining part has two (see [4]). With this choice the probability of having the same parent for two individuals is $1/(N-1)$, which behaves as $1/N$ for large N . The second rule is that any individual in the new generation chooses one parent at random in the previous one, independently on the choice of the others (see [5]). In this case the probability of having the same parent for two individuals is exactly $1/N$.

The distance between two given individuals α and β in the same generation is, by definition, the number of generations from the common ancestor. Since typical distances are proportional to N , as we are going to show, it is useful to rescale them dividing by N . Let us call $d(\alpha, \beta)$ these rescaled distances (obviously, $d(\alpha, \alpha)$ vanishes).

For two distinct individuals α and β in the same generation one has

$$d(\alpha, \beta) = d(g(\alpha), g(\beta)) + 1/N \quad , \quad (1)$$

where $g(\alpha)$ and $g(\beta)$ are the two parent individuals. The above dynamics simply state that the rescaled distance in the new generation increases by $1/N$ with respect to the parents distance (the non rescaled distance would have increased by 1). The two parents coincide with probability $1/N$ and they are distinct individuals with probability $(N-1)/N$.

By using equation (1) it is easy to show that, for $\lambda < 1$, the average over the process gives $\langle \exp(\lambda d(\alpha, \beta)) \rangle = 1/(1-\lambda)$. This result, which holds for large N , implies that the probability that $d(\alpha, \beta) = x$ is simply $\exp(-x)$. Notice that this is not the distribution of the distances inside a single large population but the average distribution sampled over many stochastically equivalent populations or, which is the same, sampled over the same population at many different times. Also notice that, according to this result, the typical non-rescaled distance is of order N (see also [4]).

According to this distribution one has that the process averages $\langle d(\alpha, \beta) \rangle = 1$ and $\langle d^2(\alpha, \beta) \rangle = 2$ which means that the distance between individuals may show huge differ-

ences for different pairs. But this is not the important point, in fact, there is another larger source of statistical dispersion for distances, as follows.

We can use again equation (1) in order to compute the quantities $\langle d(\alpha, \beta)d(\beta, \gamma) \rangle$ and $\langle d(\alpha, \beta)d(\gamma, \delta) \rangle$. To reach this goal one simply has to take into account that any of the pairs which can be formed by two of the four individuals α, β, γ and δ may have coinciding parents with probability $1/N$. The probability that more then two parents coincide is of higher order. Taking the large N limit one finds $3\langle d(\alpha, \beta)d(\beta, \gamma) \rangle = \langle d^2(\alpha, \beta) \rangle + 2\langle d(\alpha, \beta) \rangle$ and $6\langle d(\alpha, \beta)d(\gamma, \delta) \rangle = 4\langle d(\alpha, \beta)d(\beta, \gamma) \rangle + 2\langle d(\alpha, \beta) \rangle$.

Solving these simple equations one gets $\langle d(\alpha, \beta)d(\beta, \gamma) \rangle = 4/3$ and $\langle d(\alpha, \beta)d(\gamma, \delta) \rangle = 11/18$. In this form, this result only seems to state that there is a statistical correlation between distances corresponding to different pairs. But there is a much more interesting consequence. Let us introduce the mean distance of the individuals of a population as

$$d = \frac{2}{N(N-1)} \sum_{\alpha > \beta} d(\alpha, \beta) , \quad (2)$$

this is simply the average on a single population (and at a given time) of the internal distances considering all the $N(N-1)/2$ possible pairs. This quantity is random for finite N but should reach deterministically its average value for large N .

On the contrary, while the process averages $\langle d \rangle$ and $\langle d(\alpha, \beta) \rangle$ equals 1, in the thermodynamical ($N \rightarrow \infty$) limit $\langle d^2 \rangle = \langle d(\alpha, \beta)d(\gamma, \delta) \rangle = 11/18$. In other words, not only the distances are randomly distributed inside the population but their mean on all possible pairs is random even if N is extremely large. We show these facts in fig. 1 where the time evolution of the mean distance of the population is shown for $N = 2000$ which is sufficiently large to destroy all finite size effects. Looking at fig. 1, we notice that the mean distance is subject to abrupt negative variations due to the extinction of large subpopulations.

Notice that the typical size of living humanity, measured from nuclear genetic distance, corresponds to a population of 10000 individuals. Paleoanthropologists explain this fact by a recent demographic explosion which followed a bottleneck.

Since the mean distance is random, the distribution $q(x)$ of the distances in a single large population must also be random. For finite N one has that $q(x)dx$ is simply the number of pairs in a given population whose distance lies in the interval $[x, x+dx]$ divided by the total number $N(N-1)/2$ of possible pairs. Then, d is simply the average on this

distribution ($d = \int q(x) x dx$) and since d is random also $q(x)$ remains random when the infinite population limit is performed. The above definition implies $\langle q(x) \rangle = p(x)$, i. e., the average of the $q(x)$ over many independent realizations of the process is $\exp(-x)$.

The most important fact is that the distribution may be very different from the averaged one. This fact can be appreciated in fig. 2 where $q(x)$ (computed again from a population of 2000 individuals) does not show any resemblance with its average $\exp(-x)$. From fig. 2 (which is a typical one) it is clear that individuals spontaneously cluster in groups. In fact, most of the distances assume a few of values corresponding to the distances between the major subpopulations.

These genetically isolated subpopulations are not different species or geographically isolated groups, but they can originate in perfectly inter-breeding and (nuclear DNA) homogeneous populations. In fact, sexually reproducing nuclear DNA has a completely different statistics. In large populations the distance for almost all pairs of individuals coincide with the average value 1 (see also [6]).

It should also be noticed that distance between two individuals is estimated from the number of differences in mtDNA due to mutation. The number of these differences is itself stochastic and only in average is proportional to the distance. Therefore, the possibility of having large mtDNA isolation of subpopulation is even larger one can estimate here.

Let us come back now to the problem which has inspired the present work in order to have a quantitative understanding of the phenomena.

In 1997, 1999 and 2000 a team of researchers [1, 2] extracted mtDNA from three different specimens of Neandertal and was able to amplify many short strands of the hyper-variable region (HVR1 and HVR2) using Polymerase Chain Reaction (PCR). In 1997 they compared the first specimen (Feldhofer) mtDNA sequence against a database of 994 different mtDNA sequences from modern humans. Modern humans differed from each other in 8.0 ± 3.1 positions, by contrast, the Neandertal genome had 27.0 ± 2.2 differences from modern humans. In 1999, the same people successfully extracted a second mtDNA sequence from the same Neandertal fossil. This study confirmed the results of the first one, modern humans differed from each other by 10.9 ± 5.1 (range 1-35), the Neandertal differed from humans by 35.3 ± 2.3 (range 29-43). In 1999, they successfully extracted a mtDNA sequence from a second Neandertal, a 29,000 year-old fossil (Mezmaiskaya). The distance between Mezmaiskaya and a particular modern human sequence, known as the reference sequence, was 22, compared

to 27 for the first Neandertal while the two Neandertals differed from each other in 12 positions. In 2000, scientists announced the sequencing of a third Neandertal mtDNA specimen from a cave at Vindija, Croatia. The Neandertal differed from modern humans by 34.9 ± 2.4 positions.

The conclusion was that the Neandertals lie at a statistically large distance from modern humans. Results in this paper suggest this conclusion being incorrect, in fact, the situation is quantitatively the same of fig. 2, where there is a subpopulation whose distance from others is three or more times larger than the average distance and the most probable one.

Mungo Man, at variance with Neandertals, is an anatomically modern man. The fossil, 60,000 years-old, (older than the three Neandertal fossils) was discovered in 1974 in the dry bed of Lake Mungo in New South Wales, Australia. Recently Mungo Man has attracted attention due to the extraction of mtDNA from fragments of his skeleton [3]. The authors identify differences between Mungo mtDNA and living aborigines mtDNA and conclude that Mungo man belongs to a lineage diverging before the most recent common ancestor of contemporary humans. Also in this case, the argument is doubtful, in fact, as already discussed the rapid extinctions of mtDNA subpopulations are well evident in fig. 2.

The conclusion (if any) of this work is that hardly mtDNA studies can be used to prove [1, 2] 'Out of Africa' theory or disprove it [3]. On the contrary, the study of DNA distribution in living population allows for much more reliable results, especially if the study is performed on nuclear DNA which encodes information about all our ancestry. Up to now, these studies mostly support 'Out of Africa' theory in its original form or in a more recent and less extreme one [7].

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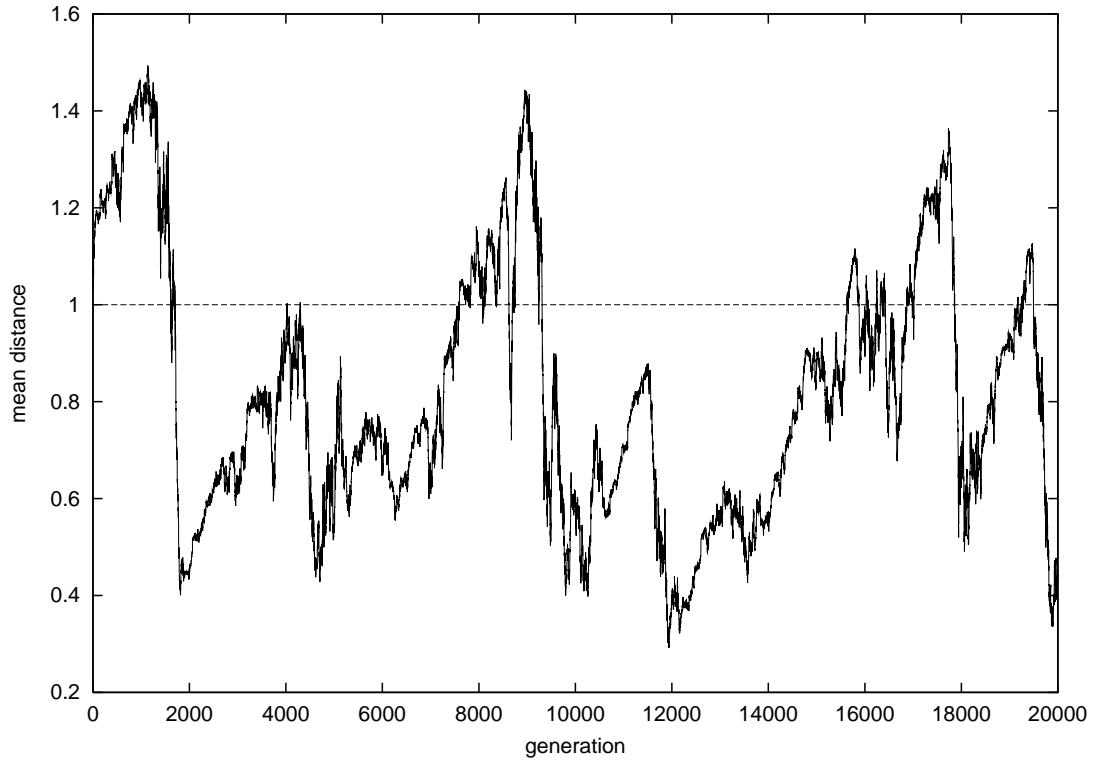


FIG. 1: Mean distance of a single population individuals as a function of time (generation). The time evolution of the mean distance is computed for $N = 2000$, which is sufficiently large to destroy all finite size effects. This quantity remains random even in the infinite population limit. Notice that the mean distance is subject to abrupt negative variations due to the extinction of large subpopulations.

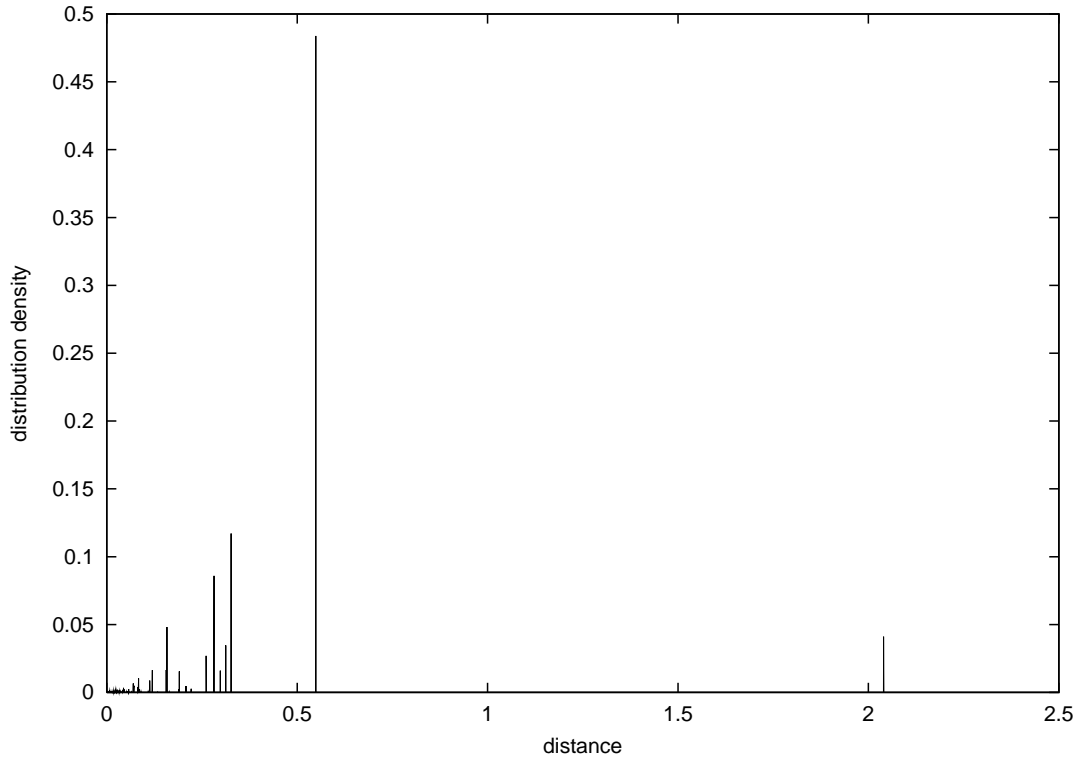


FIG. 2: Distribution density of distances in a single population. Here we compute this quantity for a population of 2000 individuals. The most important fact is that the distribution is very different from its process average $\exp(-x)$. It is clear that individuals naturally cluster in groups. In fact, most of the distances assume a few of values corresponding to the distances between the major subpopulations. Notice that the largest distances are a few time larger than average distance and most probable one.